No. 21-70670

IN THE UNITED STATES COURT OF APPEALS
FOR THE NINTH CIRCUIT

YUROK TRIBE et al.,

Petitioners,

v.

U.S. ENVIRONMENTAL PROTECTION AGENCY et al.,

Respondents.

Consolidated with No. 21-70168

ALASKA COMMUNITY ACTION ON TOXICS,

Petitioner,

v.

U.S. ENVIRONMENTAL PROTECTION AGENCY et al.,

Respondents.

Consolidated with No. 24-7497

YUROK TRIBE et al.,

Petitioners,

v.

U.S. ENVIRONMENTAL PROTECTION AGENCY et al.,

Respondents.

On Petitions for Review of Final Agency Actions of the
United States Environmental Protection Agency

BRIEF OF AMICI CURIAE PUBLIC HEALTH EXPERTS IN SUPPORT OF PETITIONERS

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INTEREST OF AMICI CURIAE

Amici, who are among the world's leading scientists, have a strong interest in protecting infants, children, and other vulnerable populations from harms associated with exposure to decabromodiphenyl ether.[1]

Amicus Aimin Chen, MD, Ph.D., is Professor of Epidemiology in the Department of Biostatistics, Epidemiology and Informatics at the Perelman School of Medicine at the University of Pennsylvania. He received an M.D. in Preventive Medicine and an M.S. in Epidemiology from Nanjing Medical University, and he has a Ph.D. in Epidemiology and Health Statistics from Fudan University. He completed postdoctoral training in Perinatal and Pediatric Environmental Epidemiology at the National Institute of Environmental Health Sciences ("NIEHS"). He is Co-Director of the National Institutes of Health ("NIH")/NIEHS-funded Philadelphia Regional Center for Children's Environmental Health and Associate Director of the Translational Research Support Core in the

[1] Amici have authority to file this brief pursuant to Federal Rule of Appellate Procedure 29(a)(2) because all parties have consented to its filing. Amici's counsel authored the brief in whole, no party or a party's counsel contributed money that was intended to fund preparing or submitting the brief, and no person contributed money that was intended to fund preparing or submitting the brief. *See* Fed. R. App. P. 29(a)(4)(E).

NIH/NIEHS-funded Center of Excellence in Environmental Toxicology at the University of Pennsylvania.

As an environmental epidemiologist, Dr. Chen's research includes informal electronic waste recycling exposure and child development; exposure to polybrominated diphenyl ethers and per- and polyfluoroalkyl substances ("PFAS") and child neurobehavioral development; developmental neurotoxicity of organophosphate ester and replacement brominated flame retardants; environmental chemical mixture exposure and child health outcomes; and environmental exposome and cognitive decline and brain MRI patterns. He has studied heavy metals, persistent organic pollutants, endocrine disrupting chemicals, and chemical mixtures. He is Associate Editor of International Journal of Hygiene and Environmental Health and on the Editorial Review Board of Environmental Health Perspectives.

Amicus Susan L. Schantz, Ph.D., is Professor Emerita in the Department of Comparative Biosciences and the Neuroscience Program at the University of Illinois at Urbana-Champaign. She received her B.A. in Psychology and Ph.D. in Environmental Toxicology from the University of Wisconsin–Madison and completed postdoctoral training in

Developmental Psychology at Wayne State University. She is Associate Director of the NIEHS-funded Research Training Program in Toxicology and Environmental Health and Contact PI of the Illinois Kids Development Study, part of the NIH Environmental influences on Child Health Outcomes Program.

As a neurotoxicologist, Dr. Schantz has led over three decades of federally funded research investigating the effects of endocrine-disrupting chemicals—including phthalates, phenols, PFAS, and organophosphate flame retardants—on brain development and cognitive function in both animal models and human cohorts. She previously directed the NIEHS-funded Children's Environmental Health Research Center at Illinois (2009–2020), where she studied prenatal exposures and neurodevelopment in children, with a focus on chemical mixtures, maternal stress, and sex-specific effects. Her work has also demonstrated how endocrine disrupting chemicals influence auditory function, seizure susceptibility, and cognitive aging. Dr. Schantz is a former Associate Editor of Environmental Health Perspectives and has published extensively in the fields of neurotoxicology and environmental health.

Amicus Heather M. Stapleton, Ph.D., is the Ronie-Richele Garcia-Johnson Distinguished Professor in the Nicholas School of the Environment at Duke University, with appointments in the Integrated Toxicology and Environmental Health Program and the Department of Civil and Environmental Engineering. She earned her B.S. in Biology and Chemistry from Southampton College and her M.S. and Ph.D. in Environmental Chemistry from the University of Maryland. She completed postdoctoral training at the National Institute of Standards and Technology.

Dr. Stapleton is an environmental chemist and exposure scientist whose research focuses on human exposure to endocrine-disrupting and emerging contaminants, including flame retardants and PFAS. She directs the Duke University Superfund Research Center, the Duke Environmental Analysis HHEAR Lab Hub, and the North Carolina Firefighter Cancer Cohort Study. Dr. Stapleton's group has pioneered the use of silicone wristbands to monitor personal chemical exposures in infants, children, adults, and companion animals. Her work investigates how exposure to semi-volatile organic compounds from consumer products and indoor environments may influence thyroid function,

neurodevelopment, and cancer risk. Dr. Stapleton has published extensively on human biomonitoring, exposure science, and environmental health—including on the impact of decabromodiphenyl ether exposure—and has served on numerous editorial boards and scientific advisory panels. Dr. Stapleton has testified before the U.S. Senate and received multiple awards for her contributions to environmental science, including the 2025 American Chemical Society Award for Creative Advances in Environmental Science & Technology.

Amicus R. Thomas Zoeller, Ph.D., is Emeritus Professor of Biology at the University of Massachusetts, Amherst. He holds a B.S. in Biology from Indiana University Bloomington and an M.A. and Ph.D. in Neuroendocrinology from Oregon State University. He did postdoctoral work in molecular neuroendocrinology at NIH in Bethesda, Maryland. His research focused on the role of thyroid hormone in brain development with an emphasis on the fetal brain and on the mechanisms by which environmental endocrine disruptors can interfere with thyroid hormone action in the brain.

During his career, Dr. Zoeller directed grants from NIEHS, the National Science Foundation, the Environmental Protection Agency, and

was most recently a contributor to the ATHENA project in the European Union. He was the recipient of the Endocrine Society Laureate Award for Outstanding Public Service, the UMass Distinguished Community Engagement in Research Award as well as the UMass Chancellor's Medal for Research. He was a member of the Environmental Protection Agency's Endocrine Disruptor Screening and Testing Advisory Committee, the Science Advisory Board and chair of the Exposure and Human Health Committee and was a member of several Federal Insecticide, Rodenticide, and Fungicide Act Scientific Advisory Panels. He was a lead writer and editor of the United Nations Environment Programme/World Health Organization's State of the Science of Endocrine Disruption. Dr. Zoeller is also an active member of the Endocrine Society, having served on several committees related to research in Endocrinology and in Endocrine Disrupting Chemicals.

INTRODUCTION

There is no dispute that decabromodiphenyl ether ("decaBDE")—a a chemical flame retardant that has been used for decades for consumer and commercial purposes—is toxic, persistent, and bioaccumulative. Congress recognized as much when it amended the Toxic Substances Control Act ("TSCA") in 2016 to require the Environmental Protection Agency ("EPA") to regulate decaBDE. *See* 15 U.S.C. § 2605(h) (requiring regulation of certain chemicals identified in the 2014 update of the TSCA Work Plan for Chemical Assessments); *see also* EPA, *TSCA Work Plan for Chemical Assessments: 2014 Update* at 4 (Oct. 2014) ("2014 Update"). But the very aspects of decaBDE that led Congress to mandate its regulation underscore EPA's failure to adequately protect the public through the regulations it eventually promulgated. *See* 1-ER-0002–0016 (EPA's 2021 rule); 1-ER-0017–0051 (EPA's 2024 amendments).[2]

As Petitioners explain in their opening brief, EPA's regulations effectively fail to regulate the recycling of decaBDE-containing plastics, the use of recycled decaBDE-containing plastics in the manufacturing of

[2] Throughout this brief, "ER" refers to the Excerpts of Record filed by Petitioners, and "Pets.' Br." refers to Petitioners' Opening Brief.

new articles, the solid waste disposal of decaBDE, the concentration of decaBDE in land-applied sewage sludge, and the wastewater discharge of decaBDE by facilities handling decaBDE-containing articles. *See* Pets.' Br. at 18–23 (describing regulations). As a result, EPA's regulations do little to eradicate the existing and continued risks posed by decaBDE.

While EPA's failures are concerning for several reasons, it is especially troubling that decaBDE can cause particularly significant and severe harms to infants and children, who are at greater risk of exposure to decaBDE than adults. The myriad risks posed by decaBDE include adverse neurological outcomes, thyroid disruption, and adverse embryo-fetal developmental outcomes, among others. What's more, the harms stemming from EPA's regulations are not limited to those caused solely by decaBDE. Through a process called "debromination," decaBDE can break down into other chemicals that are actually *more* toxic.

The scientific evidence contradicts the assertion that decaBDE is a legacy flame retardant presenting no ongoing harm. Given the robust and expanding body of scientific research, Amici are convinced that EPA's decaBDE regulations do not adequately protect human health. This Court should thus grant Petitioners' petition for review.

ARGUMENT

I. DecaBDE And Its Debrominated Derivatives

Polybrominated diphenyl ethers ("PBDEs") are compounds—referred to as "congeners"—that are used as flame retardants to reduce flammability in a wide range of consumer and industrial products.[3] There are 209 individual PBDE congeners.[4] Each congener shares the common characteristic of having a diphenyl ether sub-structure, but differs with respect to the number and placement of bromine atoms it contains around this sub-structure.[5]

DecaBDE, also referred to as BDE-209 (its technical congener identifier), is one such PBDE. Commercial decaBDE (sometimes referred to as "c-decaBDE") has been widely applied for decades as a flame retardant in electronics, appliances, textiles, furniture, and building materials like wiring, plastics, and foams. *See, e.g.*, 1-ER-0006, 0012; 2-

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[3] *See* Dorman et al., *Polybrominated Diphenyl Ether (PBDE) Neurotoxicity: A Systematic Review and Meta-Analysis of Animal Evidence*, 21 J. Toxicology & Env't Health, Part B: Critical Reviews 269 (Oct. 2018).

[4] *Id.*

[5] *Id.*

ER-0053, 0060. While commercial decaBDE contains trace amounts of other congeners, its dominant congener is BDE-209. *See* 2-ER-0168.

The widespread use of decaBDE is particularly concerning because it has "[h]igh environmental persistence" and "[h]igh bioaccumulation potential." 2014 Update at 8 (giving decaBDE the highest possible persistence and bioaccumulation score). Persistent and bioaccumulative chemicals, like decaBDE, "present special issues because organisms can remain exposed to them for a very long time." EPA, *TSCA Work Plan Chemicals: Methods Document* at 14 (Feb. 2012). In fact, because decaBDE has been used in plastics, the chemical has been identified in numerous consumer products that were created using recycled plastics—including children's toys, car seats, plastic food utensils (*e.g.*, spatulas), and food packaging materials. *See, e.g.*, 2-ER-0192; 5-ER-0977.[6]

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[6] *See also, e.g.*, Minnesota Dep't of Health, *Decabromodiphenyl ether (decaBDE)* (May 2024) ("DecaBDE can be found in household items and products such as . . . [c]hildren's products (older car seats and toys).") [hereinafter "MDH 2024"]; DiGangi & Strakova, *Toxic Toy or Toxic Waste: Recycling POPs Into New Products* (Oct. 2015) ("The data shows that OctaBDE and DecaBDE used in plastics for electronics are being recycled into plastic children's toys."); Liu et al., *From E-Waste to living Space: Flame Retardants Contaminating Household Items Add to Concern About Plastic Recycling*, 365 Chemosphere 143319 (Oct. 2024) (finding decaBDE in plastic utensils and fast food trays).

Scientific studies have found that children are at greater risk of being exposed to decaBDE.[7] This can be attributed to several factors, including children's behavior (*e.g.*, hand-to-mouth contacts),[8] and the fact that children are disproportionality exposed to decaBDE through means such as ingestion of breast milk and interaction with house dust.[9]

Children and infants are not the only population at higher risk of decaBDE exposure. For example, decaBDE exposure levels among firefighters are higher than those observed in the public generally—likely due to exposures to burning plastic products, textiles, and furniture

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[7] *See, e.g.*, Lunder et al., *Significantly Higher Polybrominated Diphenyl Ether Levels in Young U.S. Children Than in Their Mothers*, 44 Env't Sci. & Tech. 5256 (July 2010).

[8] *Id.*; Hoffman et al., *Toddler's Behavior and its Impacts on Exposure to Polybrominated Diphenyl Ethers*, 27 J. Exposure Sci. & Env't Epidemiology 193 (Mar. 2016).

[9] *See, e.g.*, 3-ER-0361–0326 (identifying three dozen studies regarding decaBDE concentration data in breastmilk); Yakout et al., *Decabromodiphenyl Ether in Breast Milk Collected from Saudi Mothers*, 35 J. King Saud Uni. Sci. 102622 (May 2023) [hereinafter "Yakout 2023"]; Fischer et al., *Children Show Highest Levels of Polybrominated Diphenyl Ethers in a California Family of Four: A Case Study*, 114 Env't Health Perspectives 1581 (May 2006) ("[H]ouse dust is considered a significant source of exposure to both lower-brominated PBDEs and BDE-209. This is especially true for children . . . ."); Wilford et al., *Polybrominated Diphenyl Ethers in Indoor Dust in Ottawa, Canada: Implications for Sources and Exposure*, 39 Env't Sci. & Tech. 7027 (Aug. 2005).

containing decaBDE.[10] And, unsurprisingly, those who work at decaBDE manufacturing plants are at higher risk of exposure to decaBDE.[11]

DecaBDE has the capacity to undergo "debromination," a chemical process in which bromine atoms are removed, resulting in the production of lower-brominated PBDE congeners. Debromination of decaBDE primarily occurs through metabolism, biodegration, or abiotic processes (*e.g.*, via sunlight exposure), and can occur in the environment as well as within living organisms after exposure.[12]

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[10] *See, e.g.*, Park et al., *High Exposure of California Firefighters to Polybrominated Diphenyl Ethers*, 49 Env't Sci. & Tech. 2948 (Feb. 2015); Levasseur et al., *Characterizing Firefighter's Exposure to Over 130 SVOCs Using Silicone Wristbands: A Pilot Study Comparing On-Duty and Off-Duty Exposures*, 15 Sci. Total Env't 155237 (Aug. 2022); Fent et al., *Flame Retardants, Dioxins, and Furans in Air and on Firefighters' Protective Ensembles During Controlled Residential Firefighting*, 140 Env't Int'l 105756 (July 2020).

[11] Chen at al., *Disruption of Thyroid Hormone Levels by Decabrominated Diphenyl Ethers (BDE-209) in Occupational Workers from a deca-BDE Manufacturing Plant*, 120 Env't Int'l 505 (Aug. 2018) [hereinafter "Chen 2018"].

[12] *See* Sun et. al, *A Critical Review on BDE-209: Source, Distribution, Influencing Factors, Toxicity, and Degredation*, 183 Env't Int'l 108410 at §5 (Jan. 2024) [hereinafter "Sun 2024"]; Stapleton et al., *Debromination of the Flame Retardant Decabromodiphenyl Ether by Juvenile Carp (Cyprinus carpio) Following Dietary Exposure*, 38 Env't Sci. & Tech. 112 (Jan. 2004); Stapleton et al., *In Vivo and in Vitro Debromination of Decabromodiphenyl Ether (BDE 209) by Juvenile Rainbow Trout and Common Carp*, 40 Env't Sci. & Tech. 4653 (Aug. 2006); Stapleton &

A review published just last year explained that decaBDE has the potential to debrominate into the following 61 additional PDBE congeners (the "Debrominated Derivatives"):[13]

- NonaBDEs: BDE-206, BDE-207, BDE-208
- OctaBDEs: BDE-194, BDE-196, BDE-197, BDE-199, BDE-201, BDE-202, BDE-203, BDE-204
- HeptaBDEs: BDE-171, BDE-172, BDE-175, BDE-176, BDE-177, BDE-178, BDE-179, BDE-180, BDE-182, BDE-183, BDE-184, BDE-187, BDE-188, BDE-190, BDE-191, BDE-193
- HexaBDEs: BDE-128, BDE-133, BDE-137, BDE-138, BDE-139, BDE-144, BDE-146, BDE-149, BDE-150, BDE-153, BDE-154, BDE-157, BDE-161
- PentaBDEs: BDE-85, BDE-92, BDE-99, BDE-100, BDE-101, BDE-102, BDE-103, BDE-118, BDE-126
- TetraBDEs: BDE-47, BDE-48, BDE-49, BDE-52, BDE-66, BDE-77
- TriBDEs: BDE-17, BDE-28
- DiBDEs: BDE-7, BDE-8, BDE-15
- MonoBDEs: BDE-3

Dodder, *Photodegradation of Decabromodiphenyl Ether in House Dust by Natural Sunlight*, 27 Env't Toxicology & Chemistry 306 (Feb. 2008).

[13] PBDE congeners are grouped by the number of bromine atoms they contain. For example, OctaBDEs have eight bromine atoms, PentaBDEs have five, and DiBDEs have two. DecaBDE is the only congener with ten.

See Sun 2024 at Fig. 5.[14] Accordingly, regulation that reduces exposure to decaBDE to the extent practicable, as TSCA requires, will address the downstream effects of decaBDE's Debrominated Derivates.

II. Exposure To DecaBDE And Its Debrominated Derivatives Is Scientifically Linked To Serious Health Risks

Scientific literature published in the past fifteen years has exposed the significant and multifaceted toxicity of decaBDE. These studies have associated decaBDE with a multitude of adverse health outcomes. Most troublingly, infants and children are particularly susceptible to many of these outcomes, including neurodevelopmental harms and thyroid disruption. Indeed, decaBDE can cause harm to fetuses *in utero* and to babies who are exposed to decaBDE-contaminated breast milk.

Beyond those harms, decaBDE has also been associated with other adverse neurotoxicity, immunotoxicity, genotoxicity, endocrine toxicity, and reproductive toxicity outcomes, and more (including increased cancer risk). Of course, these harms are just the tip of the iceberg. Because decaBDE can debrominate into 61 other congeners, the risks posed by

[14] A high-resolution photo of Figure 5 from Sun 2014 can be accessed here: https://ars.els-cdn.com/content/image/1-s2.0-S0160412023006839-gr5_lrg.jpg.

each Debrominated Derivative (many of which disproportionately affect children) are implicated by the presence of decaBDE.

a. The toxic effects of decaBDE

i. Neurotoxicity

DecaBDE's neurotoxicity—*i.e.*, its ability to cause an adverse change in the structure or function of the central and/or peripheral nervous system—is well documented in humans. DecaBDE (like other PBDEs[15]) can enter human breast milk,[16] and a "significant" inverse association has been found between decaBDE in breast milk and cognitive function.[17] Mechanistically, higher exposure to decaBDE has been found to cause neurodevelopmental toxicity *in vitro* by causing

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[15] *See, e.g.*, Talsness et al., *In Utero and Lactational Exposures to Low Doses of Polybrominated Diphenyl Ehter-47 Alter the Reproductive System and Thyroid Gland of Female Rat Offspring*, 116 Env't Health Perspectives 308 (Dec. 2007).

[16] Shi et al., *A National Survey of Tetrabromobisphenol-A, Hexabromocyclododecane and Decabrominated Diphenyl Ether in Human Milk from China: Occurrence and Exposure Assessment*, 599 Sci. of the Total Env't 237 (Dec. 2017).

[17] Chao et al., *Levels of Breast Milk PBDEs From Southern Taiwan and Their Potential Impact on Neurodevelopment*, 70 Pediatric Research, 596 (Dec. 2011).

genomic instability of cultured stem cells and decreasing DNA methyltransferase activity.[18]

Animal studies confirm decaBDE's neurotoxicity, particularly with respect to embryos and juveniles. One study showed that decaBDE altered brain development (*e.g.*, by reducing brain cell growth and altering neuron connections) in mice offspring that were exposed to the chemical *in utero*.[19] In two other studies, long-term learning deficits and memory impairment were associated with decaBDE exposure in mouse pups and juvenile rats.[20] Studies of zebrafish embryos/larvae that were exposed to decaBDE similarly associate that exposure with brain

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[18] Du et al., *DNA Methylation and Copy Number Variation Analyses of Human Embryonic Stem Cell-Derived Neuroprogenitors After Low-Dose Decabromodiphenyl Ether and/or Bisphenol A Exposure*, 37 Human & Experimental Toxicology 475 (May 2018) [hereinafter "Du 2018"].

[19] Xu et al., *Developmental Exposure of Decabromodiphenyl Ether Impairs Subventricular Zone Neurogenesis and Morphology of Granule Cells in Mouse Olfactory Bulb*, 92 Reproductive Toxicology 529 (Sept. 2017).

[20] Li et al., *Neonatal Exposure to BDE 209 Impaired Learning and Memory, Decreased Expression of Hippocampal Core SNAREs and Synaptophysin in Adult Rats*, 59 NeuroToxicology 40 (Mar. 2017); Reverte et al., *Long Term Effects of Murine Postnatal Exposure to Decabromodiphenyl Ether (BDE-209) on Learning and Memory are Dependent upon APOE Polymorphism and Age*, 40 Neurotoxicology & Teratology 17 (Nov. 2013).

structure and neural pathway changes, abnormal swimming behavior, and reduced axon growth.[21]

ii. Embryo-Fetal Developmental Toxicity

Several of the studies discussed above address decaBDE's toxicity as it affects embryos.[22] Additional animal studies further demonstrate decaBDE's association with physical defects and interference with normal fetal growth during pregnancy.[23]

For example, a study of zebrafish embryos found that high exposure to decaBDE caused physical deformities, heart problems, and delayed development.[24] Another study found that high exposure to decaBDE can

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[21] Zhu et al., *Effect of Combined Exposure to Lead and Decabromodiphenyl Ether on Neurodevelopment of Zebrafish Larvae*, 144 Chemosphere 1646 (Feb. 2016); Garcia-Reyero et al., *Effects of BDE-209 Contaminated Sediments on Zebrafish Development and Potential Implications to Human Health*, 63 Env't Int'l 216 (Feb. 2014) [hereinafter "Garcia-Reyero 2014"]. Zebrafish embryos/larvae are ideal models for assessing associations between exposure of a toxicant and developmental neurotoxicity. *See* Scholz et al., *The Zebrafish Embryo Model in Environmental Risk Assessment—Applications Beyond Acute Toxicity Testing*, 15 Env't Sci. Pollution Rsch. Inst. 394 (June 2008).

[22] *See, e.g.*, Du 2018; Garcia-Reyero 2014.

[23] *Cf.* MDH 2024 at 2 ("Some of the negative health effects seen in lab animals include . . . [p]oor fetal and infant development.").

[24] Zezza et al., *Toxicological, Gene Expression and Histopathological Evaluations of Environmentally Realistic Concentrations of*

damage placental structure and function in mice.[25] And a study of pregnant rats demonstrated that decaBDE can cross the placenta and enter breast milk, and that exposure during pregnancy may impact obesity outcomes.[26]

iii. Endocrine Toxicity

DecaBDE can also interfere with endocrine systems (particularly thyroid hormones), which are vital for brain development and growth. Indeed, decaBDE is an endocrine disrupter[27]—meaning that it "alters function(s) of endocrine systems and consequently causes adverse health effects . . . ."[28]

Polybrominated Diphenyl Ethers PBDE-47, PBDE-99 and PBDE-209 on Zebrafish Embryos, 183 Ecotoxicology & Env't Safety 109566 (Nov. 2019).

[25] Zhao et al., *Gestational Exposure to BDE-209 Induces Placental Injury via the Endoplasmic Reticulum Stress-Mediated PERK/ATF4/CHOP Signaling Pathway*, 233 Ecotoxicology & Env't Safety 113307 (Mar. 2022).

[26] Park et al., *Global DNA Methylation Patterns and Gene Expression Associated with Obesity-Susceptibility in Offspring of Pregnant Sprague-Dawley Rats Exposed to BDE-47 and BDE-209*, 49 Korean J. Clinical Lab. Sci. 28 (Mar. 2017).

[27] Costa & Giordano, *Is Decabromodiphenyl Ether (BDE-209) a Developmental Neurotoxicant?*, 32 NeuroToxicology 9 (Jan. 2011).

[28] *Endocrine Disrupter*, ScienceDirect, https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/endocrine-disruptor.

One study from 2018 found that occupational workers at a decaBDE manufacturing plant had elevated decaBDE levels that were significantly correlated with thyroid hormone levels.[29] Another found an association between long-term exposure to decaBDE and potential tumorigenic effects on the thyroid.[30] Other studies have shown similar outcomes in animals. One study found that the accumulation of decaBDE in zebrafish larvae affected thyroid hormone secretion and the expression of thyroid-related genes,[31] while another found that decaBDE exposure at environmentally relevant levels resulted in significant reductions in circulating thyroid hormone levels and substantial increases in the activity of enzymes that regulate thyroid hormones in the brain of minnows.[32]

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[29] Chen 2018.

[30] Wang et al., *Long-Term Exposure to Decabromodiphenyl Ether Promotes the Proliferation and Tumourigenesis of papillary Thyroid Carcinoma by Inhibiting TRβ*,, 14 Cancers 2772 (June 2022) [hereinafter "Wang 2022"].

[31] Chen at al., *Bioconcentration and Metabolism of Decabromodiphenyl Ether (BDE-209) Result in Thyroid Endocrine Disruption in Zebrafish Larvae*, 110 Aquatic Toxicology 141 (Apr. 2012).

[32] Noyes et al., *Low Level Exposure to the Flame Retardant BDE-209 Reduces Thyroid Hormone Levels and Disrupts Thyroid Signaling in Fathead Minnows*, 47 Env't Sci. & Tech. 10012 (July 2013).

iv. Genotoxicity

DecaBDE exposure has also been linked to genetic damage. For instance, a study that evaluated the genotoxicity of decaBDE in human neuroblastoma cells found that the chemical can cause DNA damage by inducing oxidative stress.[33] Even more problematic, decaBDE has been found to induce human embryonic stem cell death *in vitro* and the decreased expression of certain genes.[34] Similar results have been found in animal studies. A study of decaBDE's impact in neonatal rats found, among other adverse effects, a correlation with the rate of cell death, cell viability, and levels of global gene DNA methylation,[35] and another study

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[33] Pellacani et al., *Evaluation of DNA Damage Induced by 2 Polybrominated Diphenyl Ether Flame Retardants (BDE-47 and BDE-209) in SK-N-MC Cells*, 31 Int'l J. Toxicology 372 (June 2012).

[34] Du et al., *BDE-209 Inhibits Pluripotent Genes Expression and Induces Apoptosis in Human Embryonic Stem Cells*, 36 J. Applied Toxicology 659 (July 2016).

[35] Chen at al., *Assessment of the Neurotoxic Mechanisms of Decabrominated Diphenyl Ether (PBDE-209) in Primary Cultured Neonatal Rat Hippocampal Neurons Includes Alterations in Second Messenger Signaling and Oxidative Stress*, 192 Toxicology Letters 431 (Feb. 2010).

found that decaBDE exposure can harm dolphins' mitochondrial structure and cell signaling.[36]

v. Reproductive Toxicity

DecaBDE exposure has also been associated with adverse reproductive function outcomes. One 2019 study in mice found that decaBDE exposure resulted in damage to testicular physiological structure, cell death in testis, decreased sperm count and motility, and increased sperm malformation rates.[37] Subsequent studies on animals have found similar correlations between decaBDE and male reproductive

[36] Rajput et al., *Polybrominated Diphenyl Ethers Exert Genotoxic Effects in Pantropic Spotted Dolphin Fibroblast Cell Lines*, 271 Env't Pollution 116131 (Feb. 2021).

[37] Li et al., *BDE-209 Induces Male Reproductive Toxicity Via Cell Cycle Arrest and Apoptosis Mediated by DNA Damage Response Signaling Pathways*, 255 Env't Pollution 113097 (Dec. 2019).

toxicity.[38] DecaBDE induces oxidative stress,[39] for instance, which can disrupt sperm integrity and testicular chromatin.[40] DecaBDE has also been associated with estrogenic activity, which can cause reproductive problems.[41]

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[38] *See, e.g.*, Li et al., *BDE-209 and DBDPE Induce Male Reproductive Toxicity Through Telomere-Related Cell Senescence and Apoptosis in SD Rat*, 146 Env't Int'l 106307 (Jan. 2021) (decaBDE exposure led to decline of sperm quality and quantity in rats, possibly caused by cell senescence and apoptosis in testis); Zhang et al., *Decabromodiphenyl Ether Induces Male Reproductive Toxicity by Activating Mitochondrial Apoptotic Pathawy Through Glycolipid Metabolism Dysbiosis*, 285 Chemosphere 131512 (Dec. 2012) (decaBDE caused sperm abnormality via cell apoptosis in rats); Li et al., *DNA Methylation Changes Induced by BDE-209 are Related to DNA Damage Response and Germ Cell Development in GC-2spd*, 109 J. Env't Scis. 161 (Nov. 2021) (decaBDE may affect cell growth and sperm development in mice).

[39] Tseng et al., *Postnatal Exposure of the Male Mouse to 2,2',3,3',4,4',5,5',6,6'-decabrominated Diphenyl Ether: Decreased Epididymal Sperm Functions Without Alterations in DNA Content and Histology in Testis*, 224 Toxicology 33 (July 2006).

[40] *See, e.g.*, Omran et al., *Potential Hazards of Bisphenol A Exposure to Semen Quality and Sperm DNA Integrity Among Infertile Men*, 81 Reproductive Toxicology 188 (Oct. 2018).

[41] Chen et al., *High-Throughput Transcriptome Sequencing Reveals the Combined Effects of Key E-Waste Contaminants, Decabromodiphenyl Ether (BDE-209) and Lead, in Zebrafish Larvae*, 214 Env't Pollution 324 (July 2016).

vi. Immunotoxicity

Studies further correlate decaBDE with weakened immune function, which in turn makes it more difficult to fight disease and regulate inflammation responses. A 2021 study in mice found that decaBDE exposure could cause immunotoxicity, possibly caused by the atrophy of the spleen and thymus, changing immunity indices, and altering gene expression.[42] Another study found that decaBDE can impair the immune response of dolphins.[43] And an additional study demonstrated that decaBDE exposure caused adverse effects on the functionality and quantity of immune cells in mice.[44]

vii. Other Toxicities and Associated Cancer Risks

In addition to the many toxicities linked to decaBDE that are discussed above, decaBDE exposure is also correlated to negative health

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[42] Liao et al., *Short-Term Exposure of Decabromodiphenyl Ether in Female Adult Balb/c Mice: Immune Toxicity and Self-Recovery*, 342 Toxicology Letters 26 (May 2021).

[43] Ying et al., *Immune Stimulation Effect of PBDEs Via Prostaglandin pathway in Pantropical Spotted Dolphin: An* In Vitro *Study*, 254 Chemosphere 126717 (Sept. 2020).

[44] Zeng et al., *Long-Term Exposure to Decabrominated Diphenyl Ether Impairs CD8 T-Cell Function in Adult Mice*, 11 Cellular & Molecular Immunology 367 (Apr. 2014).

effects of vital organs like the liver, kidneys, intestines, and heart. For example, recent studies have concluded that decaBDE exposure has adverse effects on growth performance in chickens and possible toxic effects on the liver and kidney;[45] disrupts glycolipid metabolism in the livers of mice;[46] causes intestinal toxicity in mice;[47] affects the metabolism in the rat liver and kidney, causing issues such as severe renal edema, hepatocyte spotty necrosis, and hepatic perivasculitis;[48] and can cause cardiovascular injury and endothelial dysfunction in rats.[49]

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[45] Liu et al., *Effects of Decabrominated Diphenyl Ether Exposure on Growth, Meat Characteristics and Blood Profiles in Broilers*, 11 Animals 565 (Feb. 2021).

[46] Zhu et al., *Decabromodiphenyl Ether Disturbs Hepatic Glycolipid Metabolism by Regulating the PI3k/AKT/GLUT4 and mTOR/PPAR gamma/RXR alpha Pathway in Mice and L02 Cells*, 763 Sci. Total Env't 142936 (Apr. 2021).

[47] Shaoyong et al., *BDE-209 Caused Gut Toxicity Through Modulating the Intestinal Barrier, Oxidative Stress, Autophagy, Inflammation, and Apoptosis in Mice*, 776 Sci. Total Env't 146018 (July 2021).

[48] Yang et al., *Alterations of Endogenous Metabolites in Urine of Rats Exposed to Decabromodiphenyl Ether Using Metabonomic Approaches*, 26 J. Env't Sci. 900 (Apr. 2014).

[49] Jing et al., *Cardiovascular Toxicity of Decabrominated Diphenyl Ethers (BDE-209) and Decabromodiphenyl Ethane (DBDPE) in Rats*, 223 Chemosphere 675 (May 2019).

DecaBDE is also associated with cancer risks. In 2008, EPA itself described decaBDE as a "suggestive" human carcinogen.[50] Subsequent studies also suggest that decaBDE may increase the risk of cancer. In 2014, for instance, a study suggested that decaBDE has carcinogenic potential for a variety of tumors due the positive correlation between its exposure and groups of genes associated with various cancer types.[51] More recent studies have found that decaBDE exposure is associated with thyroid cancer[52] and may be a liver carcinogen.[53]

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[50] EPA, *Toxicological Review of Decabromodiphenyl Ether (BDE-209)* (June 2008); *see also* 3-ER-0427 ("The studies presented demonstrate evidence of carcinogenicity of DecaBDE.").

[51] Li et al., *Toxic Effects of Decabromodiphenyl Ether (BDE-209) on Human Embryonic Kidney Cells*, 5 Frontiers in Genetics 118 (May 2014).

[52] Zhang et al., *Plasma Polybrominated Diphenyl Ethers, Urinary Heavy Metals and the Risk of Thyroid Cancer: A Case-Control Study in China*, 269 Env't Pollution 116162 (Jan. 2021); *see also* Wang 2022; Hoffman et al., *Exposure to Flame Retardant Chemicals and Occurrence and Severity of Papillary Thyroid Cancer: A Case-Control Study*, 107 Env't Int'l 235 (Oct. 2017).

[53] Yuan et al., *AhR-Mediated CYP1A1 and ROS Overexpression are Involved in Hepatotoxicity of Decabromodiphenyl Ether (BDE-209)*, 352 Toxicology Letters 26 (Nov. 2021).

b. The health risks posed by decaBDE's Debrominated Derivatives are well-documented.

But exposure to decaBDE is not the only source of harms implicated by EPA's decaBDE regulations. As discussed above, decaBDE can debrominate into 61 additional PBDE congeners. *See supra* 12–14. Thus, to the extent EPA's regulations allow decaBDE exposure—for example, by failing to meaningfully regulate the recycling of decaBDE—those regulations have *also* failed to protect the public from risks associated with the Debrominated Derivatives. As one study aptly put it: "Increased exposure to BDE-209 raises health concerns since its breakdown may result in lower brominated congeners and/or other products, which are more toxic than the parent compound."[54]

There is a vast amount of scientific literature concerning the harms associated with the Debrominated Derivatives. While Amici could fill the entirety of a separate brief identifying and discussing those studies, they instead highlight the following literature that reviews studies of the risks posed to children, infants, and fetuses by exposure to the Debrominated Derivatives:

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[54] Yakout 2023.

- Gibson et al., *Effects of Polybrominated Diphenyl Ethers on Child Cognitive, Behavioral, and Motor Development*, 15 Int'l J. Env't Rsch. & Pub. Health 1636 (Aug. 2018) (reviewing epidemiological evidence of correlation between infant and child development and prenatal exposure to PBDEs, and finding a negative association between PBDE concentrations and neurodevelopment);

- Lam et al., *Developmental PBDE Exposure and IQ/ADHD in Childhood: A Systematic Review and Meta-Analysis*, 125 Env't Health Perspectives 86001 (Aug. 2017) (concluding that there is sufficient evidence supporting an association between reduced IQ and exposure to developmental PBDE);

- Vuong et al., *Flame Retardants and Neurodevelopment: An Updated Review of Epidemiological Literature*, 7 Current Epidemiology Report 220 (Nov. 2020) (reviewing studies indicating that PBDEs are neurotoxic, particularly for gestational exposures, and are associated with behavioral problems and reduced cognition in children); and

- Vuong et al., *Exposure to Polybrominated Diphenyl Ethers (PBDEs) and Child Behavior: Current Findings and Future Directions*, 101 Hormones & Behavior 94 (May 2018) (concluding that PBDE exposure during fetal development is associated with poorer attention control and executive function impairments in children).

Accordingly, adequate decaBDE regulation would better protect children and infants from the risks posed by decaBDE's Debrominated Derivatives.[55]

[55] Protecting children is, of course, an intrinsically noble cause. However, it is worth noting that research has shown that the reduction of children's chemical exposures also provides societal and economic benefit. *See, e.g.*, Gaylord et al., *Trends in Neurodevelopmental Disability Burden Due to*

CONCLUSION

As the scientific literature identified and discussed in this brief demonstrates, the health harms posed by decaBDE and its Debrominated Derivatives are real, significant, and numerous. By failing to adequately regulate the recycling, disposal, and discharge of decaBDE, EPA has ensured that the public—and vulnerable populations such as children and infants—will be exposed to toxic harms for decades to come.

This Court should grant Petitioners' petition for review.

Early Life Chemical Exposure in the USA From 2001 to 2016: A Population-Based Disease Burden and Cost Analysis, 502 Molecular & Cellular Endocrinology 110666 (Feb. 2020) (quantifying cost of IQ points lost and cases of intellectual disability attributable to PBDE exposure).

CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limit of Federal Rule of Appellate Procedure 29(a)(5) because, excluding the parts of the document exempted by Federal Rule of Appellate Procedure 32(f), it contains 5,191 words.

This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type-style requirements of Federal Rule of Appellate Procedure 32(a)(6) because it has been prepared in a proportionally spaced typeface using Microsoft Word in Century Schoolbook 14-point font.

/s/ Evan Bianchi
Evan Bianchi